ISRCTN29062676 https://doi.org/10.1186/ISRCTN29062676

A programme to develop a skin patch containing two medicines (physostigmine and hyoscine) - study 2: Assessment of blood levels of the two medicines and any associated symptoms in healthy male participants wearing four prototype skin patches

Submission date
30/08/2019

Recruitment status
No longer recruiting

Registration date
06/09/2019

Overall study status
Completed

Last Edited
06/09/2019

Condition category
Injury, Occupational Diseases, Poisoning

[ ] Prospectively registered
[ ] Protocol
[ ] Statistical analysis plan
[ ] Results
[ ] Individual participant data
[ ] Record updated in last year

Plain English summary of protocol

Background and study aims
Several different versions (called formulations) of a skin patch containing two medicines (physostigmine and hyoscine) have been developed. The skin patch releases these medicines enabling them to cross the skin into the bloodstream. The aim of this study was to measure the amount of physostigmine and hyoscine in the blood at different times over a 72 hour period and assess any associated symptoms.

Who can participate?
Study participants were healthy males aged between 18 and 40 years

What does the study involve?
The plan was for each subject to wear three different patch sizes of their allocated formulation in turn for 72 hours, with start dates for each application being separated by at least two weeks. On each occasion blood samples were taken before and after patch application to measure the amounts of the two medicines (physostigmine and hyoscine). In addition the activity of the enzyme acetylcholinesterase (AchE) was measured in these blood samples. The effects of the patch were assessed by recording the condition of the skin under the patch at set times and any symptoms that were experienced. Heart rate, blood pressure, electrical activity of the heart (ECG), tests of vison and cognitive function were also recorded at set times.

What are the possible benefits and risks of participating?
There were no direct individual benefits for the subjects participating. However, the information collected from these individuals added to the scientific knowledge about the physostigmine and hyoscine patch. All medicinal products have a risk of causing side effects. The most common side

effects known about the medicines in the patch are nausea and vomiting due to physostigmine and blurred vison and dry mouth due to hyoscine. All formulations of patches tested were considered well tolerated.

Where is the study run from?
The study was conducted at Simbec Research Limited

When is the study starting and how long is it expected to run for?
The study has been completed.

Who is funding the study?
The study was funded by UK MoD

Who is the main contact?
centralenquiries@dstl.gov.uk

Contact information

Type(s)
Scientific

Contact name
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Additional identifiers

EudraCT/CTIS number
2004-005029-23

IRAS number

ClinicalTrials.gov number
Nil known

Secondary identifying numbers
RD 209/24055

Study information

Scientific Title

A Dose-escalation Study to Investigate the Safety, Tolerability, Pharmacokinetics and Pharmacodynamics of Four Transdermal Patch Formulations (F4-F7) of Hyoscine and Physostigmine in Healthy Male Subjects

Study objectives
The aim of this study was to investigate the safety, tolerability, pharmacokinetics and pharmacodynamics of single and multiple applications of four patch formulations (F4-F7) of hyoscine and physostigmine in healthy male subjects

Ethics approval required
Old ethics approval format

Ethics approval(s)
Approved, 13/01/2005, South East Wales Local Research Ethics Committees (LREC) (Churchill House, 17 Churchill Way, Cardiff, CF10 2TW; 02920402402), ref: 04/WSE02/179

Study design
Randomised double-blind parallel dose-escalation three-period study

Primary study design
Interventional

Secondary study design
Randomised controlled trial

Study setting(s)
Other

Study type(s)
Other

Participant information sheet
No participant information sheet available

Health condition(s) or problem(s) studied
Potential risk of poisoning by nerve agent

Interventions
1. Generic drug name- physostigmine and hyoscine (transdermal patch). Four versions of PHP transdermal patch were tested. These patches contained different amounts of physostigmine and hyoscine in one of two adhesive matrices.
2. Dosage - three different patch sizes of four patch formulations (F4, F5, F6, F7) were tested. Each subject received one of four formulations of transdermal patches, with six subjects allocated to each formulation.
Each subject received three applications of that formulation (one each of three different patch sizes in order of increasing size)

Data collection - Safety monitoring, blood sampling for pharmacokinetics and pharmacodynamics, patch adhesion and patch application site assessments, ECG and ocular function assessments were performed for up to 96 hours after the application of each patch.

Method of measurements:
Hyoscine and Physostigmine: liquid chromatography-tandem mass spectrometry (LC-MS-MS)
Acetylcholinesterase: spectrophotometry

Added 06/09/2019:
Process for randomisation of patients.
A sequential three-digit subject number was assigned once eligibility for the study had been confirmed. Subjects were randomised to receive one of the four formulations (F-4, F-5, F-6, F-7) in Period 1, and to receive the same formulation in Periods 2 and 3. Treatment was allocated according to the randomisation schedule produced by Simbec Research Limited.

Intervention Type
Drug

Phase
Phase I

Drug/device/biological/vaccine name(s)
Physostigmine, hyoscine

Primary outcome measure
Safety and tolerability of physostigmine/hyoscine combination measured using safety monitoring, blood sampling for pharmacokinetics and pharmacodynamics, patch adhesion and patch application site assessments, ECG and ocular function assessments were performed for up to 96 hours after the application of each patch

Secondary outcome measures
None

Overall study start date
16/03/2004

Completion date
30/05/2006

Eligibility

Key inclusion criteria
Subjects had to meet all of the following criteria:
1. Ability to give written informed consent prior to study participation
2. Healthy Caucasian male subjects aged between 18 and 40 years (inclusive)
3. Body Mass Index (BMI) within the range of 21 and 30 kg/m2
4. Vital signs within the following ranges:
4.1 Pulse rate 40-90 bpm
4.2 Systolic blood pressure 90-140 mmHg
4.3 Diastolic blood pressure 50-90 mmHg
5. Ability to communicate well with the Investigator and to comply with the requirements of the study

Participant type(s)

Healthy volunteer

Age group
Adult

Lower age limit
18 Years

Sex
Male

Target number of participants
24 healthy male subjects

Key exclusion criteria
1. Presence of any clinically significant medical condition as determined by the Investigator
2. Any surgical or medical condition which might have significantly altered the absorption, distribution, metabolism or excretion of any drug. (e.g. renal or liver disease, respiratory, immunological, endocrine or neurological disorders)
3. Any ECG abnormality other than sinus bradycardia or respiratory sinus arrhythmia
4. Known or suspected hypersensitivity or idiosyncratic reaction related to any of the study products
5. Any history of contact dermatitis
6. Plasma cholinesterase genotype homozygous for A or S variant
7. Any skin disorder, broken skin, scars, tattoos at the sites of patch application (i.e. on both arms)
8. Glaucoma or a history of glaucoma in first degree relatives (i.e. parents, siblings or offspring)
9. Presence of Anterior Chamber Narrow Angle (Van Herrick Grade 1 and 2)
10. Intra-ocular pressure exceeding 20 mm Hg
11. Uncorrected vision in both eyes of worse than 6/9 on the Snellen Scale
12. Required glasses or contact lenses for distance vision
13. Peripheral visual fields outside of age corrected normal parameters
14. History of asthma (within the previous 10 years), exercise induced bronchospasm or relevant seasonal bronchospasm
15. Lung function of less than 80% of predicted spirometry criteria
16. History or evidence of drug abuse (opiates, methadone, cocaine, amphetamines, methamphetamines, cannabinoids, barbiturates)
17. Positive test for HIV, hepatitis B or hepatitis C
18. History or evidence of alcohol abuse defined as an intake of more than 28 units per week (4 units per day), where 1 unit corresponds to 250 ml beer, 20 ml spirits/liqueur or one glass (100 ml) of wine
19. Positive urine test for alcohol
20. Participation in another clinical study within three months prior to Screening
21. Use of any prescription medication within 21 days prior to Baseline
22. Use of non-prescription medication within 7 days prior to Baseline (apart from paracetamol)
23. Donation of blood or blood products for a period of 3 months prior to or the intention to donate blood or blood products within 3 months after completion of the study

Date of first enrolment
13/01/2005

Date of final enrolment
08/04/2005

Locations

Countries of recruitment
United Kingdom

Wales

Study participating centre
Simbec Research Limited
Merthyr Tydfil
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CF48 4DR

Sponsor information

Organisation
Defence Science and Technology Laboratory (Dstl)

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Sponsor type
Government

ROR
https://ror.org/04jswqb94

Funder(s)

Funder type
Government

Funder Name

Study conducted on behalf of UK Ministry of defence

Results and Publications

Publication and dissemination plan
At present our publication plans are not confirmed as the PHP development program is ongoing. If a specific date is required, we suggest a year after the clinical trial summary is accepted by ISRCTN.

Intention to publish date
30/08/2020

Individual participant data (IPD) sharing plan
The datasets generated during and/or analysed during the current study are not expected to be made available as subject consent for their release was not obtained.

IPD sharing plan summary
Not expected to be made available